

**Human Physiology**  
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**Week - 01**  
**Lecture - 05**

Welcome everyone to another class of Human Physiology, myself Dr. Sudip Mukherjee. So, you remember in the last class we have discussed about the ion transport, it was the first class of ion transport and mostly we covered the diffusion process right. So, it was like simple diffusion we covered, facilitated diffusion we covered and if you remembered what is diffusion? Diffusion is movement of the molecules ions from high concentration to low concentration of the area without involvement of any energy. It is basically a movement of molecules or ions from outside cells to inside cells or vice versa, but to remember there is no involvement of energy. In this class, we will discuss about the ion transport through the active transport pathway.

That means, whatever the transport we discuss, energy will be involved to it. So, involvement of ATP is crucial component of active transport and why energy is required because it moves the molecule from a low concentration gradient to high concentration gradient. So, let us discuss what is active transport. So, active transport is the movement of molecules across a semipermeable membrane from lower concentration of those molecules to higher concentration of the molecule.

Why it is needed? Of course, we will discuss, but because this is happening against the concentration gradient right, you can see like if a ion moves from low to high concentration it is happening against their concentration gradient and for this reason what we need we need ATP because this is not a natural concentration gradient. So, the molecules will not move as it needs a certain energy and who supplies the energy ATP supplies the energy. So, active transport is heavily dependent on the energy. There is two type of active transport process present in our body one is the primary active transport and another is the secondary active transport. In cases of primary active transport the processes directly use the ATP for movement of the molecules from low concentration to high concentration gradient and this transporter or the whole overall transport molecule has an enzyme called ATPase what ATPase does the ATPase breaks down ATP to ADP because it needs energy.

So in the process of breaking down ATP to ADP it involves the active transport of certain ions and by this the third phosphate bond generated this helps creation of energy for movement of the process then secondary active transport is also present we will discuss after discussing all the active transport methodology after that we will discuss the secondary active transport. So, some examples we will discuss about primary active transport, the first one is sodium potassium ATPase, you can see the first one is sodium potassium ATPase. So, what is happening let us try to understand in the last class if you remember. All these diffusions, especially the facilitated diffusion through the leaky pores, the voltage gated channels, the mechanically gated channels, what all were doing? The resultant of those if you remember sodium ion, many of those cases sodium ion which is high outside of the cells and they are low inside of the cell those ions were diffused inside right because those were regular simple or facilitated diffusion they cause lot of sodium ions to accumulated inside of the cell which is certainly not good because we also remember we discussed that if sodium concentration gets higher inside of the

cell, what it attracts? It attracts water. So, sodium attracts water with it and eventually it can cause the cells to burst.

So, we need a counteractive machinery to remove this excess sodium from the cells and that this sodium potassium ATPase pump does. You can see it has like three binding site for the three sodium ion. Contrary to it, in the outside part of the cell, it has only two potassium ion. So, what will happen with the help of ATP? Three sodium ion will get removed out from the cells and contrary to it only two potassium ion will be accepted by the cells. So, in this way the cell will eject out excess sodium from the cells that was initially accumulated by various diffusion process.

So, you understand now like how important the sodium-potassium ATPS pump is. And in many neuronal cell line, muscle cells, nephron cells, everywhere you name any cell, this is one of the most important primary active transporter system. And we will slowly discuss when we will go to all those organ one by one you will see like how these primary active transport pump of sodium potassium ATPase has an important role for those organ functions. Now, let us discuss about few drugs or role of drugs or hormones effect on these sodium potassium ATPase pump right. So, insulin as you remember, we said that insulin has an important role for glucose regulation in our body, right.

So, what insulin does it basically also influences the expression of glut receptors, if you remember well, right. So, how insulin basically plays role to transport glucose or for the cellular internalization of the glucose it helps to increase the level of sodium potassium ATPS. So, what insulin does it basically increases the performance of the sodium potassium ATPS pump and what sodium potassium ATPase form require for their function it requires ATP. So, cells starts to utilize glucose more and more to produce the ATP to keep on performing the function and then as cells need more glucose the blood will transport more glucose to the cell in this way insulin will be able to distribute the glucose towards the cell. So, whenever in the body there is an excess condition of glucose, insulin tries to transport the glucose to the cells and it helps to overexpress the GLUT4 receptor and also by the overexpression or overperformance of the sodium potassium ATPase pump, it activates its process.

Next one is the thyroid hormone. Thyroid hormone also can increase the activity of the sodium, potassium, ATPase pump. This is also another very important hormone for many of the metabolism function, we will discuss in detail later. But if somebody just think about a condition that in our body if the thyroid hormone level What will observe? We observe high heat. Why so? Because thyroid hormone increases the sodium potassium ATPase pump and by doing that it requires lot of energy involvement to that and with energy heat also generates.

So, insulin and thyroid hormone it influences the sodium potassium pump, but digoxin This is an important drug we will discuss. This is given to the cardiac arrest patient. It helps to inhibit the sodium potassium ATPase pump and it also helps in terms of increasing the contractility of the heart. So, its detailed mechanism the digoxin and how it actually increases the contractility of the heart we will discuss in the slide number 14 in today's class only. But just remember from this slide the takeaway message is that insulin thyroid hormone influences the activation of the sodium potassium ATPases pump contrary to it digoxin inhibits the pump.

The next set of primary active transport will discuss is the calcium ATPase pump. So, if you remember generally calcium is what generally calcium is like high outside the cell and it is low inside of the cell right. This is in general condition, but this primary active transport of calcium

ATPase pump, we have to think and discuss about a specific area which is muscle cells. So, in terms of muscle cells, we will discuss about the calcium ATPase pump. So, what is present in muscle cells if you remember we have sarcoplasmic reticulum is a very important component of muscle cells why because this is a storage house of the calcium.

So, muscle cell are the storage house of calcium inside of sarcoplasmic reticulum. But in the cytoplasm generally in the cytoplasm of the muscle cells what you will see will see a lack of calcium ion present. So, in low calcium ion in the cytoplasm, but high inside of the sarcoplasm. So, what happens if the calcium ATPase pump gets activated or when it needs to function? Basically, calcium ion moves from low concentration of cytoplasm to high concentration of sarcoplasmic reticulum area. This will basically move any excess calcium ion from the cytoplasm to the sarcoplasmic causing the muscle relaxation because if there is no calcium present in the cytoplasm, they will not be able to bind with muscle protein and create this contraction mechanism.

I hope you understood. I will again recap maybe very quickly. So, sarcoplasmic reticulum has higher concentration of calcium and SR membrane has this calcium ATPase pump that helps to kind of push the calcium ion from cytoplasm to SR. We have low calcium in the cytoplasm, so this ion moves from low to high with the help of ATP. It increases as a whole the calcium ATPase pump, it increases the sympathetic nervous system activity which increases the level of norepinephrine and epinephrine.

We'll discuss this again later, but just remember that they together further increases the intracellular process by increasing the protein kinase A. Protein kinase A further stimulates calcium ATPase. So, this is kind of a close loop action, right. So, in cases of sympathetic nervous system, certain molecules like nor-epinephrine, epinephrine, they get secreted, they stimulate this PK, protein kinase A. The protein kinase A further stimulates the calcium ATPase pump, right.

So, I hope you understood. The next one is equally important, it is the secondary active transport. So, what is happening like ideally in cases of active transport molecules are moving from low concentration to the high concentration area and it requires the involvement of energy or ATP. This is mainly happening for the primary active transport right. It involves also the participation of an enzyme called ATPase.

But in cases of secondary active transport you can see there is indirect use of ATP what does it mean, that the primary component of the secondary active transport that doesn't require the ATP but to execute the secondary active transport we also need to first perform the primary active transport. So, what I am trying to say is like, secondary transport is dependent on the primary active transport. Now, the primary active transport is dependent on the ATP, right. So, although secondary active transport does not directly need ATP for its ion transport process, but because it is correlated with the primary active transport indirectly it also uses ATP. So, any type of active transport either be it primary or secondary eventually will require energy or ATP.

Now, what happens sodium molecules, they move from high concentration to low concentration for the secondary active transport and they act as a piggyback kind of system. So, what basically it will do, sodium ion will take another ion, for example, it can be chlorine, it can be potassium, it can be glucose and will help to bring that ion along with the sodium. So, eventually in cases of secondary ion transport sodium plays an important role because without the movement of the sodium the secondary transport will not happen. So, the first secondary

active transport we will discuss is the sodium glucose symporter. So, you should see this name very important it is symporter.

What does mean that sodium and glucose both the ion is moving in the same direction. So, in cases of secondary active transport both sodium and glucose both are moving towards the same direction from outside to inside of the cells. Let's think of a specific condition like kidney cells. What is happening in the kidney cells? Glucose is low outside and high inside of the kidney cell. Now, by process of this sodium-potassium-ATPS primary transport, what is happening? Initially, sodium is building higher outside of the cells, right, because sodium is kind of moving out of the cells by the primary active transport and it is getting built outside.

So as the sodium ion gets build up outside what you can see you can see that sodium ion concentration becomes higher outside of the cell and it becomes lower inside of the cells what it will do then, it will facilitate a diffusion process. I hope you understood again. I will recapitulate quickly. So, what we are trying to say that primary active transport like the sodium ATPase pump, what it does, it removes 3 sodium ions out of the cell and it only accepts 2 potassium ions. So, as it is removing lot of sodium ions outside of the cells, obviously, sodium ions gets higher outside and it becomes lower inside that facilitates a diffusion in cases of secondary active transport.

And while sodium comes inside it helps the glucose to bind with the sodium just you think that sodium has a binding site for the glucose and it will carry the glucose along with it and bring inside of the cells and that's why because both sodium and glucose is coming together in the same direction we call it as a sodium glucose symporter okay so in this way glucose from inside kidney cells get reabsorbed in the blood. Now, let's discuss about a specific condition or a specific drug. This is like SGLT-2 inhibitor. So, what will it inhibit? It will basically inhibit the sodium glucose importer pump. So, what is basically it will happen? In cases of diabetes, do we really need the glucose reabsorption? Answer is no, right? Because in cases of diabetes already we are high with the glucose concentration in the blood all the time because the insulin regulation is faltered.

There might be like even insulin resistance in our body. Maybe our pancreatic beta-islet cells are not properly functioned in that cases we are already have like high reach concentration of glucose So we do not need any further deabsorption in the kidney. What we need basically we need that glucose to remove from the urine and to do that what we will do we will use the SGLT-2 inhibitor. So basically SGLT-2 inhibitor will stop the sodium glucose symporter pump. It will basically stop the sodium glucose symporter pump and if it stops the sodium glucose symporter pump, no glucose will get further reabsorbed from kidney to blood and if the glucose molecules build up here and don't get reabsorbed, what will happen? It will come out from the urine.

So, any type of diabetic patient doctor can recommend SGLT2 type of inhibitor that basically stops sodium glucose importer pump stopping any reabsorption of glucose and by which we can easily remove the excess glucose out of the body. Then another important secondary active transport pump is the sodium potassium chloride symporter. Same way, it also needs the facilitation of the sodium potassium ATPase pump because for all these secondary active transport process, the primary active transport process is necessary. You remember right because once the primary active transport process happen, 3 sodium ion goes out of the cell and that means it starts like building up the sodium concentration outside the cell and when it happens concentration gradient creates from outside to inside sodium ion comes in same way

chloride is also high outside and low inside of the cell so with the sodium chloride or ion also comes inside of the cell and now together both sodium and chloride facilitates the movement of potassium potassium is generally low outside of the cells and high inside of the cells So, using this secondary active transport, you can understand how sodium and chloride act as kind of a piggyback type of system and helps potassium to come inside of the cell, okay. Where we can see this type of symporter, sodium potassium chloride symporter, you can see this in loop of Henle in the kidney cells, okay.

Let's discuss quickly about a drug function, which is diuretics. So, what is happening in case of diuretics, right. In cases of kidney problem, maybe the kidney is unable to kind of filter the water probably, maybe in the body lot of water accumulation is happening. So, we do not want the water to get all those ions like sodium, potassium, chloride to get reabsorbed in the body. Why so? Because sodium ion attracts water, right? So, sodium ion basically attracts water along with it.

So, if sodium gets reabsorbed In cases of kidney failure, what will happen? It will also attract water with it in the blood and already due to kidney failure, maybe there is a edema condition, lot of fluid accumulation happens. So, you do not want to retain excessive fluid in the body. We want the water to get out. So, in this cases, doctor will prescribe the diuretics. What diuretics will do? It will basically shut off the sodium potassium chloride symporter pump causing no more reabsorption of these ions from loop of Henle to the blood and which will also stop any type of reabsorption of water.

So, basically excess water will come out through the urine. Hopefully, you understood it. The last one is the secondary active transport, the sodium hydrogen pump antiporter. This is also present in the kidney cells. Same way, the sodium potassium ATPase primary active transport pump will build up the sodium concentration outside and from the high concentration of sodium to low concentration of sodium inside of the cells, the ion will move.

This time it is little bit different. The sodium is not exactly taking the hydrogen ion along with it. The hydrogen ion movement is now this time opposite to sodium ion. That's why we'll call these as a antiporter pump. You see like hydrogen ion is more in this case and hydrogen moves from inside of the kidney cell to the lumen against their concentration gradient because hydrogen is more inside of the kidney cell and in the blood of the lumen it is low. So, eventually hydrogen from the kidney cell, it will move out to the lumen against its concentration gradient.

It happens where? It happens in the distal convolute tubule of the kidney, DCT of the kidney area. Let us see the action of aldosterone. What aldosterone does? high level of aldosterone increases the activity of the sodium potassium, sodium sorry, sodium hydrogen pump, sodium hydrogen antiporter pump in the DCT. So, if it increases the activity of sodium hydrogen pump in DCT, what will happen? More and more number of hydrogen or the like acidic ion mostly the H plus ion will move from the kidney cells to the lumen or eventually in the blood and what will happen? It will lead to the more H plus ions in urine leads to metabolic alkalosis. In this case, lower level of aldosterone has low activity in the sodium hydrogen pump that makes blood more acidic and causes a condition of metabolic acidosis okay finally we'll discuss about this is very important we'll discuss about sodium calcium antiporter pump and here we'll connect about the function of digoxin So what is happening same way sodium calcium antiporter pump is dependent on the sodium potassium ATPase primary transport pump that will help to build up the sodium concentration outside of the cells and whenever there is a increase in the sodium concentration outside of the cell because of the primary active transport.

In the next step sodium will come inside from low to high concentrations through their concentration gradient and this case calcium will go out of the cells from low concentration to high concentration. Okay, so it is very important because sodium is going from high to low, from outside to inside and then the calcium ion movements is happening again in the opposite direction. That's why we are calling this term as the antiporter pump. This pump is present mostly in the heart tissues. So, let's see cases of a drug which is called digoxin.

This is given, I said like digoxin is given to the cardiac patient. Whenever there is a cardiac arrest, we give digoxin to the patient. What digoxin does? Digoxin inhibits sodium potassium ATPase pump. If you remember in the active transport class, we mentioned in a brief line that digoxin inhibits the sodium potassium ATPase pump. So, what will happen if digoxin inhibits the sodium potassium ATPase pump, the 3 sodium which gets removed from the cell, it will not happen, this will stop.

So, basically the sodium concentration will not build outside of the cells, this process will get stopped by the action of digoxin. Then it will significantly hamper the secondary active transport of the sodium calcium antiporter pump right because to cause this secondary active transport for any secondary active transport the primary active transport is most important. So if the digoxin inhibits this primary active transport then the sodium calcium secondary active transport also will not happen. very important right hope you understand and if the secondary transport will not happen what will happen what is basically it is doing right if you think in the muscle this is the acer, sarcoplasmic reticulum what it has, it has high number of or a high amount of calcium ions inside and in the cytoplasm we have low amount of calcium ions. right so with the sodium potassium or sodium calcium secondary active transport pump generally calcium from low cytoplasm it goes to the high calcium concentration in the sarcoplasmic reticulum but if digoxin is given to the patient, this will not happen right and if this basically stops in the heart muscle What will happen? This calcium will be retained in the cytoplasm.

This calcium will be slowly retained. It will start slowly building it in the cytoplasm. So, due to the activity of digoxin, what we are doing? We are basically inhibiting the sodium potassium ATPase pump thus slowly building the calcium in the cytoplasm of the heart muscle cells and what it will cause if calcium deposits and get stored and accumulated in the cytoplasm, it will activate the contraction of the muscle. So, heart muscle will contract more, it will cause like a pumping of the heart better and probably the patient who was suffering from a heart failure or a cardiac arrest will get respite by the action of faster heart beat and contraction. So, this is the whole kind of mechanism how digoxin can be used for cardiac arrest patient.

Hope you understood that. So, there is one task for you. Please write down the differences between the passive and active transport. Last two classes, we discussed different modes of passive transport and different modes of active transport. So, you can do this exercise, right and thank you again for attending this very two interesting classes of ion transport. We hope that you enjoyed the class. We will come with again another new class with you in very soon. Thank you again.